Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Claims 39-47 and 49-51 are pending in this application and are rejected on various grounds. Claims 39-41 have been canceled without prejudice or disclaimer. The rejections to the presently pending claims are respectfully traversed.

Claim Rejections – 35 U.S.C. §101 and U.S.C. §112, First Paragraph

Claims 39-47 and 49-51 remain rejected under 35 U.S.C. §101 allegedly for lack of specific, substantial and credible asserted utility or a well established utility.

Claims 39-47 and 49-51 further remain rejected under 35 U.S.C. §112, first paragraph, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The Examiner maintained that "the assay fails to provide any explanation regarding a correlation of this assay and any real life diseases" and that "use to induce inflammation was not considered to be a substantial, real-world use...While particular irritants may have uses that stem from that irritant capability, in the absence of further characterization of what type of reaction the substance causes what the systemic effects of such are, the result remains a preliminary one, necessitating substantial further research....". For the reasons described below, Applicants respectfully traverse.

In the previous response, Applicants had provided arguments to show that the instantly claimed proinflammatory molecule is not an irritant. Further, without acquiescing to the propriety of this rejection, merely to expedite prosecution in this case, Applicants hereby file an executed Declaration by Sherman Fong, Ph.D., an expert in the field of immunology, who discusses the skin vascular permeability assay, the mechanism for vascular permeability, how this assay identifies proinflammatory molecules, how the assay and its modifications have been widely used in the art, by several investigators, to identify various well-established proinflammatory molecules like blood coagulation factor XIII, VEGF, etc. As Dr. Fong explains in his declaration,

> "Proinflammatory molecules can directly or indirectly cause vascular permeability by causing immune cells to exit from the blood stream and move to the site of injury or infection. These proinflammatory molecules recruit cells like leukocytes which includes monocytes,

macrophages, basophils, and eosinophils. These cells secrete a range of cytokines which further recruit and activate other inflammatory cells to the site of injury or infection. How leukocytes exit the vasculature and move to their appropriate destination of injury or infection is critical and is tightly regulated. Leukocytes move from the blood vessel to injured or inflamed tissues by rolling along the endothelial cells of the blood vessel wall and then extravasate through the vessel wall and into the tissues (see Exhibit B). This diapedesis and extravasation step involves cell activation and a stable leukocyte-endothelial cell interaction."

In this assay, proinflammatory molecules display blemishes of a previously injected marker dye, a positive exemplary exhibit of which is shown in Exhibit I. As the Fong declaration adds, the results were further analyzed by histopathological examination to rule out inflammation due to endothelial cell damage or mast cell degranulation. Hence, the vascular permeability observed for PRO326 was not due to histamine release or endothelial cell damage. Utilities for PRO326 molecule, based on a positive score in the skin vascular permeability assay, such as, to treat inflammatory diseases like autoimmune diseases, psoriasis, etc. are also discussed by Dr. Fong in his declaration. Such utilities would readily be understood, appreciated and accepted by those skilled in the art at the effective filing date as a substantial, credible and specific utility.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejections under 35 U.S.C. §101 and §112, first paragraph.

Claim Rejection – 35 U.S.C. §112-Written Description

Claims 39-43 and 50-51 were rejected under 35 U.S.C. §112, first paragraph, allegedly for lack of possession of the invention.

Applicants have canceled claims 39-41, 48 and 52-54 without prejudice or disclaimer, and hence this rejection is moot with respect to these claims. Without acquiescing to the propriety of this rejection, Applicants have amended the pending claims to recite a functional recitation: "wherein said polypeptide induces an inflammatory response." Further, Example 14 of the Written Description Guidelines issued by the U.S. Patent Office which clearly states that "protein variants meets the requirements of 35 U.S.C.§112, first paragraph as providing adequate written description for the claimed invention even if the specification contemplates but does not exemplify variants of the protein if (1) the procedures for making such variant proteins is routine

in the art, (2) the specification provides an assay for detecting the functional activity of the protein and (3) the variant proteins possess the specified functional activity and at least 95% sequence identity to the reference sequence". Based on these guidelines, Applicants submit that the instant specification evidences the actual reduction to practice of a full-length native human PRO326 polypeptide of SEQ ID NO: 294, with or without its signal sequence and of the nucleic acid of SEQ ID NO: 293. In addition, the specification provides detailed description about the cloning of variants and describes the skin vascular permeability assay for testing the encoding polypeptides. Thus, Applicants submit that the genus of nucleic acids that code for the polypeptide of SEQ ID NO: 294 or variants of nucleic acid of SEQ ID NO: 293 with 95% similarity and further, which possess the functional property that it is "wherein said polypeptide induces an inflammatory response" would encompass a genus that meets the requirements of 35 U.S. C. §112, first paragraph as providing adequate written description.

Thus, one of skill in the art would know that Applicants had possession of the invention, as described in the instantly amended claims, and therefore request that this rejection be withdrawn. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (Attorney's Docket No. **39780-1618 P2C27**). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: November 5, 2004

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